C17

Molly Leitner Advisor(s): Salvador Dura-Bernal Ph.D.

Co-author(s): -

Linking Neuronal Channelopathies to Circuit E/I imbalances and Neurodevelopmental Disorders in a Multiscale Model of Motor Cortex

Neurodevelopmental disorders (NDDs) such as epilepsy, autism spectrum disorder, and developmental delays vary greatly clinically and often impair social interaction, speech, and cognitive development. The hallmark of these disorders is an imbalance in excitatory/inhibitory input (E/I), which leads to dysfunction in neuronal circuits during development. Disorders in which the activity of neuronal ion channels become altered, known as brain channelopathies, are particularly attractive for studying E/I imbalance because their function can be directly linked to neuronal excitability. Ion channels play a vital role in generating the electrical activity in neurons and disruptions to their normal activity are highly associated with NDDs. Studying channelopathies in single cells is a robustly established procedure, however, studying how specific channel mutations affect the neuronal circuit requires a much more complicated protocol. Using a previously published primary motor cortex (M1) model, we utilize a large-scale, highly detailed biophysical neuronal simulation to investigate how channel mutations affect individual and network neuronal activity. These simulations can provide a mechanistic understanding of the role of channelopathies in E/I imbalance and how they contribute to NDD pathology. Using the M1 cortical column simulation, we measured how channel biophysical changes affect the overall excitability of the network and changes in neuronal population firing patterns to better understand the pathophysiology of the simulated channelopathy. This model provides a tool for modeling specific channelopathy cases and also exploring the effects of known pharmacological agents to return E/I balance in a time and cost efficient manner. This will allow us to better understand therapeutic targets that specifically target disease symptoms and possibly unveil novel therapeutics that can be translated clinically.